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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER

ROBINSON, P

ART UNIT

PAPER NUMBER

1653

DATE MAILED:

01/04/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/345,815

Applicant(s)

UCKUN, FATIH M.

Examiner

Patricia A Robinson

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-- The MAILING DATE of this communication appears on the cover sheet with the corresponding address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-14 is/are pending in the application.
- 4a) Of the above claim(s) 2,3,6-8 and 14 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☐ Claim(s) ____ is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☒ Claims 1-14 are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some * c) ☐ None of the CERTIFIED copies of the priority documents have been:
1. ☐ received.
2. ☐ received in Application No. (Series Code / Serial Number) ____.
3. ☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

- 14) ☒ Notice of References Cited (PTO-892)
- 15) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 16) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4.
- 17) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 18) ☐ Notice of Informal Patent Application (PTO-152)
- 19) ☐ Other: _____

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DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

- I. Claims 1-7 and 11-14, drawn to the process for inhibiting the activation of c-jun in mammalian or avian cells and therapeutic use, classified in class 435, subclass 4 and 6.
- II. Claims 1, 4, 5, 8 and 11-13, drawn to a generic protein utilized in inhibiting the activation of c-jun in mammalian or avian cells, classified in class 514, subclass 2.
- III. Claims 1, 4, 5, 9-13, drawn to the use of a quinazoline compound of formula I to inhibit the activation of c-jun in mammalian or avian cells, classified in class 514, subclass 257, 254, or 260.

The inventions are distinct, each from the other because of the following reasons:

Group I of this application contains claims directed to the following patentably distinct species of the claimed invention: ara-c, class 536/27.21; topoisomerase II inhibitor, class 514/412, 628 or 177; ultraviolet radiation, class 8/115.2; an alkylating agent, class 532/2 and ionizing radiation, class 204/157.44 .

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, there is no generic.

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Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

During a telephone conversation with Robert Harris on 11/9/99 a provisional election was made with traverse to prosecute the invention of Group III, claims 1, 4, 5, 9-13. Applicant in replying to this Office action must make affirmation of this election. Claims 2, 3, 6-8 and 14 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

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DETAILED ACTION

Oath/Declaration

It identifies the citizenship of the inventor as Turkey on one copy and the United States on another copy, please clarify and supply appropriate oaths/declarations as necessary.

Drawings

The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they are incorrectly referenced in the description: Brief Description of the Figures does not correspond to the referenced figure numbers. Correction is required.

Claim Objections

Claim 5 is objected to because of the following informalities: claim language is identical to claim 4. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claim 1 is rejected under 35 U.S.C. 112, 2nd paragraph as being incomplete. The claim recites the process of "contacting" the cells with a substance but fails to teach the effective amount of substance required to generate the desired outcome, i.e., inhibiting the activity of the Janus family kinase 3 (JAK-3). Thus the claim as written is

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incomplete, and fails to comply with requirements of 35 U.S.C. 112, 2nd paragraph.

Claims 4 and 5 are rejected under 35 U.S.C. 112, 2nd paragraph as being unclear. As both claim are identical, you can not tell what distinction applicant is intending to make between them.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 9 and 10 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Myers et al. Myers et al. discloses the results from a SAR study examining the inhibitory effect of quinazoline-based compounds on several species of tyrosine kinases. See abstract and page 417. In particular, Myers et al. discloses a base compound, 6,7- dimethoxyquinazolinone, and tests a myriad of different moieties at different positions. See page 418. Myers et al. discloses a 4-hydroxyphenyl moiety with the 6,7- dimethoxyquinazolinone backbone and in addition teaches the importance of an amine linker for enhanced inhibitory effect. See page 418-419. Finally, Myers et al. states, "The accompanying paper demonstrates that fine-tuning for selectivity vs. other tyrosine kinases is possible using a quinazoline as a template." See page 420. Thus, it would have been clearly anticipated to take the teachings of Myers et al. and further fine

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tune the compound and test its effectiveness against other members of the genus of tyrosine kinases. Disclosure of a species will anticipate a claim to a genus and further, a reference that clearly names the claimed species anticipates the claim no matter how many other species are named in that reference.

Therefore, claims 9 and 10 are rejected as being clearly anticipated by the reference Myers et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a), which forms the basis for all obviousness rejections, set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or non-obviousness.

Claims 1, 4-5, and 11-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Karin, et al, "AP-1 Function and Regulation", Cell Biology, 9:240-246, in view of Riedy et al., "Genomic Sequence, Organization, and Chromosomal Localization of Human JAK-3", Genomics 37: 57-61 and Chae, et al "Role of Tyrosine

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Phosphorylation in Radiation-induced Activation of c-jun Protooncogene in Human Lymphohematopoietic Precursor Cells", Cancer Research 53:447-451.

Applicant claims a method of inhibiting c-jun activation by contacting the cells with a substance that inhibits the activity of Janus family kinase 3 (JAK-3).

In Karin et al. c-jun and c-fos are disclosed as both belonging to the same family of transcription factors. Karin et al. states further that very stable heterodimer structures are formed between c-jun and c-fos and that the two factors are simultaneously over expressed during osteosarcoma formation. Indicating an in vivo cooperation between c-jun and c-fos. Karin et al. goes still further to teach that c-jun is expressed in response to UV radiation and cytokine exposure, and that exposure activates the p38 and Jun amino terminal kinases (JNKs). See pages 240-242. Karin et al. teaches the fact that c-jun is required for fibroblast proliferation, and that the level of c-jun gene expressed in a cell is shown to increase in response to stimuli, including cytokines and UV radiation. Id. In addition, activating proteins (AP-1), including c-jun and c-fos, play a role in cell apoptosis as evidenced in the increased expression of c-jun and c-fos in response to various stresses, including UV irradiation. See pages 243-244. Karin et al. discloses that c-jun also plays a role in ceramide-induced apoptosis, where JNK activation is essential for induction of apoptosis due to JNK's ability to induce c-jun transcription. Id. Finally, Karin et al. teaches that inhibition of AP-1, i.e. c-jun, blocks apoptosis and that AP-1 may play a role in providing a protective function in response to stresses such as UV irradiation in fibroblasts. Karin et al. does not teach the use of a specific inhibiting

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compound of JAK-3 as a means of inhibiting c-jun activation, nor does it teach the B-lymphocyte application in particular, merely fibroblasts in general.

Riedy et al., "Genomic Sequence, Organization, and Chromosomal Localization of Human JAK-3", *Genomics* 37: 57-61 teaches the activation of JAK-3 by cytokines in B-cells. See pages 58-59. While, Rose and Karin et al., "Ultraviolet Light and Osmotic Stress: Activation of the JNK Cascade Through Multiple Growth Factors and Cytokine Receptors", *Science*, 374:1194-1197 teaches the activation of tyrosine kinases and induced expression of cytokines by ultraviolet irradiation. See pages 1194-1195. In addition, Rose and Karin et al. also teach tyrosine kinase inhibitors block c-jun induction by ultraviolet light. See page 1194.

Chae, et al "Role of Tyrosine Phosphorylation in Radiation-induced Activation of c-jun Protooncogene in Human Lymphohematopoietic Precursor Cells", *Cancer Research* 53:447-451 teaches protein tyrosine kinase activation as preceding and mandating radiation induced activation of c-jun protooncogene expression B-lymphocyte cells. See Abstract and page 447.

It would have been obvious to one of ordinary skill in the art at the time Applicant's invention was made to utilize a Janus kinase inhibitor to prevent the activation of the c-jun protooncogene in response to cellular stress. The literature demonstrates that JAK activation, and in particular JAK-3, precedes and has regulatory power over the induction of c-jun protooncogene expression. Thus, it would have been

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prima facie obvious that by inhibiting JAK-3, one could mediate the expression of c-jun downstream.

Claims 9-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Karin et al. as applied to claims 1, 4 and 5 and 11-13 above, and further in view of Myers et al.

Claims 1, 4-5 and 9-13 are rejected and no claims are allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Kurosaki, "Molecular Mechanisms in B-cell Antigen Receptor Signaling", Immunology 9:309-318; Chen, et al., "The Role of c-Jun N-terminal Kinase in Apoptosis Induced by Ultraviolet C and Gamma Radiation", Journal of Biological Chemistry, vol. 271:50, pp. 31929-31936; Myers, et al., "The synthesis and SAR of new 4-(N-alkyl-N-phenyl) amino-6,7-dimethoxyquinazolines and 4-(N-alkyl-N-phenyl) aminopyrazolo [3,4-d] pyrimidines, inhibitors of CSF-1R tyrosine kinase activity", Bioorganic and Medicinal Chemistry Letters, vol. 7, No. 4, pp. 421-424; US Patent No. 5,770,603; US Patent No. 5,770,599; US Patent No. 6,004,791; US Patent No. 5,798,374; US Patent No. 5,883,110; EP Application 566,226 A1 and EP Application 602,851.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A Robinson whose telephone number is 703-305-0096. The examiner can normally be reached on 7:30 - 4:30 Monday - Friday.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 703-308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-305-7401 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

PAR
December 29, 1999

Christopher S. F. Low
Supervisory Patent Examiner
CHRISTOPHER S. F. LOW
PRIMARY EXAMINER
GROUP 1800/600